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	DB=PGPB,	USPT,USOC,EPAB,JPAB,DWPI; PLUR=Y	ES; OP=ADJ
	L6	L5 and apoe4 and transgenic	42
	L5	435/455,463,320.1,325.ccls.	35986
	L4	L3 and apoe4	13
	L3	800/18,3,9,13,13,21,22.ccls.	1798
	L2	apoe4 with transgenic	40
	L1	apoe4 near transgenic	8

END OF SEARCH HISTORY

FILE 'CAPLUS, MEDLINE, EMBASE, BIOSIS, LIFESCI' ENTERED AT 16:24:36 ON 09 NOV 2005 85 S APOE4 WITH TRANSGENIC 11 S L1 AND (THR OR ARG OR THREONINE OR ARGININE)
4 DUP REM L2 (7 DUPLICATES REMOVED) L2 L3 L4 4 S L1 AND 61 L5 1 DUP REM L4 (3 DUPLICATES REMOVED) 78 S L1 AND HUMAN L6 L7 31 S L6 AND PY<=2001 L8 14 DUP REM L7 (17 DUPLICATES REMOVED) L9 938 S WEISGRABER K?/AU L10 11 S L1 AND L2 L11 0 S L9 AND L1 L12 205 S L9 AND APOE4 12 S L12 AND TRANSGEN? 4 DUP REM L13 (8 DUPLICATES REMOVED) 1217 S FARESE R?/AU L13 L14 L15 L16 8 S L15 AND APOE4 L17 4 DUP REM L16 (4 DUPLICATES REMOVED) L18 39 S RAFFAI RO?/AU L19 13 S L18 AND APOE4

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6 DUP REM L19 (7 DUPLICATES REMOVED)

10 DUP REM L22 (11 DUPLICATES REMOVED)

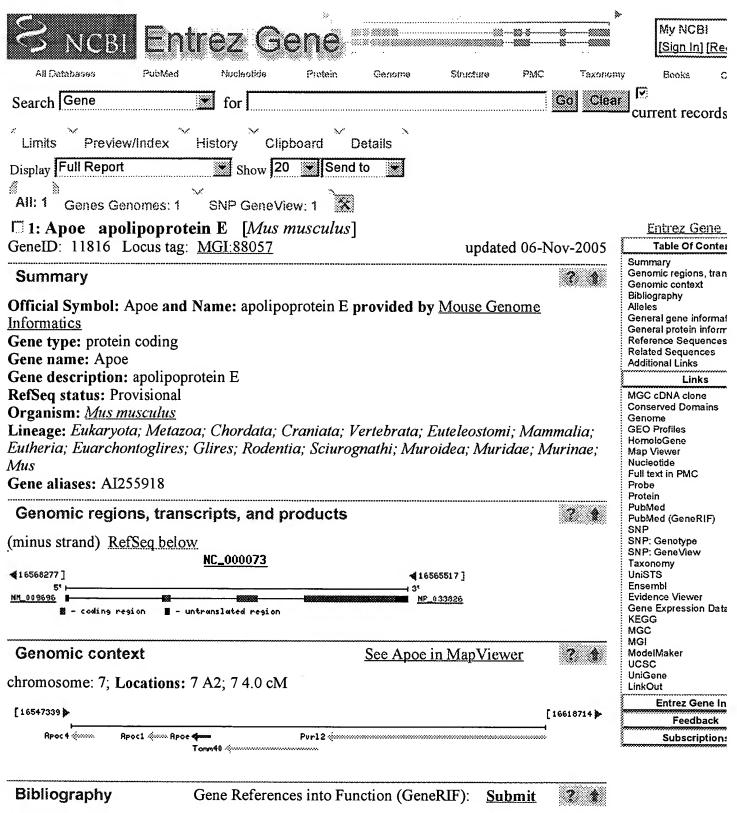
1900 S DONG LI?/AU

21 S L21 AND APOE4

L20

L21 L22

L23



PubMed links

GeneRIFs:

1. Scarb1/apoE knockout mice have coronary heart disease not involving lymphocytes

PubMed
PubMed

2. ApoE mediates the presentation of serum-borne lipid antigens and can be secreted by antigen presenting cells as a mechanism to survey the local environment to capture antigens or to transfer microbial lipids from infected cells to bystander APCs

3. ApoE4 mice develop a constellation of changes that mimic the pathology associated with human age-related macular degeneration	<u>PubMed</u>
4. protein engineering studies show that a destabilized conformation promotes apoE4 lipid binding	<u>PubMed</u>
5. additive effects of apoE and clusterin on influencing amyloid-beta deposition 6. A cholesterol-independent role of apolipoprotein E in atherosclerosis regression is critical for lipid removal from the fibrotic component of the plaque but not from the foam cell-rich layer beneath the endothelium.	PubMed PubMed
7. Human CRP transgene expression is thus up-regulated in apoE-deficient mice, apparently reflecting altered estrogen levels, despite the absence of other systemic signs of inflammation	<u>PubMed</u>
8. In addition to the effect of apoE on lipid trafficking, apoE may also influence the astroglial response to damage	<u>PubMed</u>
9. Chronic renal failure aggravates atherosclerosis in apoE(-/-) mice.	<u>PubMed</u>
10. ApoE has a physiologic role as a regulator of osteoblast function	PubMed
11. Effects of a standardized freeze-dried powder made from fresh grapes on the	PubMed
development of atherosclerotic lesions in apolipoprotein E deficient mice.	<u> </u>
12. Increased atherosclerosis is accompanied by increases in VCAM-1 and P-	PubMed
selectin levels in the two apoE(-/-) mouse strains, the high HDL level may protect	1.110111100
against atherosclerosis by inhibiting the expression of adhesion molecules in	
BALB/c.apoE(-/-) mice.	
13. autoregulation of the LXRalpha gene facilitates induction of apoE in mouse	PubMed
adipose tissue	<u>i doivioa</u>
14. important in HSV-1 colonization of ovaries	PubMed
15. In a mouse model of restenosis, a subphysiological level of apoE was	PubMed
associated with beneficial effects on lesion size/composition. ApoE has a generally	1 401/104
important protective function in the arterial wall.	
	PubMed
by physiologic regulators of insulin sensitivity.	<u> </u>
17. Improvement in insulin resistance induced by a high-fat diet, in apoe knockout	PubMed
mice of vasculopathy. did not alter plaque composition,	***************************************
18. activation of extracellular signal-regulated kinase has a role in increasing tau	<u>PubMed</u>
phosphorylation in apolipoprotein E4 transgenic mice	
19. Deficiency of apoE protein in macrophages attenuates the ingestion of apoptotic	PubMed
cells in vitro and results in impaired clearance of apoptotic cell remnants and a functionally relevant systemic proinflammatory condition in vivo.	
20. Intravital microscopy of the common carotid artery revealed a significantly	<u>PubMed</u>
greater number of leukocytes rolling on the vessel walls in apoE-/-pGI receptor-/-	
mice.	
21. The apoE4 isoform of apolipoprotein E (apoE), which is the major genetic risk	<u>PubMed</u>
factor of Alzheimer disease.	
22. plays a significant role in host defense against candidiasis.	<u>PubMed</u>
23. Review. This review will examine our present understanding of the pathology	<u>PubMed</u>
and progression of plaques in Apo-E-deficienct mice and highlight some of the	
nutritional, pharmacological, and genetic studies that have enhanced this	
understanding.	
24. ApoE3 has a role in liver expression of fatty acid binding protein, as shown in	<u>PubMed</u>
transgenic mice models	
25. apoE metabolism requires ABCA1 protein in the central nervous system	<u>PubMed</u>
26. Results describe the relative roles of apolipoprotein E isoforms in low density	<u>PubMed</u>
lipoprotein receptor (LDLR)- and non-LDLR-mediated very low density	
lipoprotein (VLDL) clearance.	
27. The accelerated renal injury that was observed in diabetic apo E-KO mice was	<u>PubMed</u>
attenuated by approaches that inhibit renal AGE accumulation.	

28. serum chemokine levels are potential markers for atherosclerosis susceptibility in C3H and C57BL apoE(-/-) mice fed on a normal rodent diet	<u>PubMed</u>
29. uremia markedly accelerates atherogenesis in apolipoprotein E-deficient mice. 30. Results show that alterations in DNA methylation profiles are early markers of atherosclerosis in an apolipoprotein E-null mouse model and may play a causative role in atherogenesis.	PubMed PubMed
31. Knockout mice are at risk for cognitive deficits. 32. Apolipoprotein E promotes astrocyte colocalization and degradation of deposited amyloid-beta peptides.	PubMed PubMed
33. After sirolimus treatment, the cholesterol content of the aortic arch was reduced in apoe knockout mice compared to normal controls.	<u>PubMed</u>
34. estradiol facilitates neurite growth through an ApoE-dependent mechanism. 35. Low plasma apoE (1-3 x 10(-8) M) suppresses atherosclerosis by as yet undefined mechanisms, not dependent on the presence of apoA-I or HDL or an increased capacity of serum acceptors for Free Cholesterol efflux	PubMed PubMed
36. ApoE deficient mice had significantly increased lymphocyte proliferation responses to both myelin antigens and mitogens and significantly more infiltrating lesions in the central nervous system (CNS) in histopathology	PubMed
37. generation and characterization of two transgenic mouse lines expressing human ApoE2 in neurons and glial cells	<u>PubMed</u>
38. use of a model of conditional gene repair to examine metabolism 39. Conditional disruption of the peroxisome proliferator-activated receptor gamma gene in mice results in lowered expression of ABCA1, ABCG1, and apoE in macrophages and reduced cholesterol efflux.	PubMed PubMed
40. modulating transport of polyunsaturated phospholipid molecular species in synaptic plasma membranes.	<u>PubMed</u>
41. Results identify the cyclooxygenase-2 gene as a target of APOE signaling, link HDL and APOE to prostacyclin receptor IP action, and describe a potential new basis for the cardioprotective effect of HDL and APOE.	<u>PubMed</u>
42. ApoE normally associates with acetylcholinesterase in the synaptic cleft of slow muscles, modulating the activity of the enzyme and therefore quantal size.	PubMed
43. neuronal expression of apoE is regulated by a diffusible factor or factors released from astrocytes	<u>PubMed</u>
44. impact of telomere attrition on atherogenesis induced by dietary cholesterol in apolipoprotein E (apoE)-deficient mice	<u>PubMed</u>
45. In aged female apoÉ0/0 mice water maze performance was impaired with search strategies. In parallel, increased corticosterone concentrations were measured in apoE0/0 mice in response to novelty and during the circadian cycle.	<u>PubMed</u>
46. Lack of both NPRA and apoE synergistically enhances cardiac hypertrophy, suggesting roles for Npr1 as well as Apoe in regulation of hypertrophic cell growth.	<u>PubMed</u>
47. Results demonstrate that apoE4-202 functions even in the presence of clearance-defective apoE2.	<u>PubMed</u>
48. isoform-specific role in mediating the systemic and brain inflammatory responses	<u>PubMed</u>
49. TR4 can also regulate apolipoprotein E, C-I, and C-II gene expression via the	<u>PubMed</u>
TR4 response element within the hepatic control region 50. Brain regional differences in the production of apoE throughout the estrous cycle were noted. Exogenous estradiol has regionally specific effects on apoE expression. Regional variability appears to vary as a function of the estrogen receptor subtype	PubMed
51. role in Alzheimer's disease-like neurodegeneration and behavioral deficits in transgenic mice	PubMed
52. apoE inhibits cell migration via cAMP-dependent protein kinase A activation as a consequence of its binding to LRP-1	<u>PubMed</u>

53. After adoptive regulatory T cells type 1 transfer in female apolipoprotein E-knockout mice, developing atherosclerotic plaques had fewer macrophages and T cells than plaques of control mice	<u>PubMed</u>
54. apoE deficiency in apoE knockout mice leads to a deficit in olfactory function, suggesting an important role for apoE in the olfactory system	<u>PubMed</u>
55. ApoE(-/-)/IL-4(-/-) mice showed a 58% and 64% decrease in disease in aortic arch compared to apoE(-/-)/IL-12(-/-) mice, respectively, and a 78% decrease in thoracic lesions compared to apoE(-/-)/IL-12(-/-).	<u>PubMed</u>
56. Apolipoprotein E facilitates cerebral amyloid angiopathy and spontaneous hemorrhage in amyloid precursor protein transgenic mice.	<u>PubMed</u>
57. ApoB-48 and apoB-100 differentially influence the expression of type-III hyperlipoproteinemia in APOE*2 mice	<u>PubMed</u>
58. adrenal gland cholesterol metabolism in apolipoprotein E deficient mice	PubMed
59. lack of lipoprotein receptor-related protein 5 and apolipoprotein E is seen in	
	<u>PubMed</u>
severe hypercholesterolemia, impaired fat tolerance, and advanced atherosclerosis	Diag
60. recycling of apolipoprotein E in primary cultures of mouse hepatocytes	<u>PubMed</u>
61. Following complete spinal cord transection Apo-E is upregulated in neutrophils	<u>PubMed</u>
and macrophages at the injury site and is found at later times in astrocytes during	
remodeling of white matter tracts, notably in degenerating parts of the fasciculus	
gracilis.	
62. Apolipoprotein E deficiency promotes increased oxidative stress and	<u>PubMed</u>
compensatory increases in antioxidants in brain tissue.	
63. The increase in apoE expression closely correlated in time and spatial	<u>PubMed</u>
distribution with axonal and neuronal degeneration, consistent with a role as an	
'injury-response' protein	
64. Transgenic mice deficient in apoE display altered levels of mature amyloid	<u>PubMed</u>
precursor protein (APP) as well as increased amounts of both beta-cleaved C-	
terminal fragments and Abeta peptides.	
65. Mice lacking apoE appear not to be impaired in spatial memory per se but are	<u>PubMed</u>
deficient in a procedural component of the Morris water maze.	5
66. The effect of angiotensin II on arterial wall stiffness in apolipoprotein E knockout mice.	<u>PubMed</u>
	7X-1-X 4'- 1
67. involvement of ApoE in the hematogenous route of HSV-1 to the CNS	PubMed Data d
68. Peroxisome proliferator-activated receptor alpha, gamma coagonist LY465608 inhibits macrophage activation and atherosclerosis in apolipoprotein E knockout	PubMed
mice	
69. in null mice, blockade of platelet-derived growth factor or its receptors	DohMad
transiently delays but does not prevent fibrous cap formation	<u>PubMed</u>
70. The data indicate a neuroprotective role for estrogen in global ischemia, the	PubMed
mechanism of which is apoE-dependent	<u>i doivica</u>
71. regulated expression of gene cluster in macrophages	PubMed
72. regulation of macrophage ApoE expression and processing by extracellular	PubMed
matrix	*******************
73. helps maintain blood brain barrier; of particular importance after brain injury	<u>PubMed</u>
74. Apolipoprotein E4 potentiates amyloid beta peptide-induced lysosomal leakage	PubMed
and apoptosis in neuronal cells	
75. Reconstituted discoidal ApoE-phospholipid particles are ligands for the	<u>PubMed</u>
scavenger receptor BI	
76. ApoE affects the age of onset of Abeta deposition in amyloid precursor protein	<u>PubMed</u>
transgenic mice as well as the level, structure and anatomic distribution of brain	
Abeta deposits	
77. Apo-E knockout middle cerebral artery occlusion mice showed a worsened	<u>PubMed</u>
deficit in locomotor activity, which was significantly correlated with exacerbated cortical lesion volume	
COLLICAL ICSIOII VOLUINE	

Alleles ?

The following allele types are documented at Mouse Genome Informatics (MGI)

- Targeted (knock-in) (1) PubMed
- Targeted (knock-out) (3) PubMed

General gene information

2 1

Markers

Apoe(e-PCR) (Links: UniSTS: 141112)

Alternate name: MGI:1205863

AI255918(e-PCR) (Links: <u>UniSTS: 179533</u>)

Alternate name: 392587

PMC186328P2(e-PCR) (Links: UniSTS: 271700)

GeneOntology

Provided by MGI

Function	Evidence	
heparin binding	IEΑ	
lipid binding	IEA	
lipid transporter activity	ŒΑ	
lipoprotein binding	IDΑ	<u>PubMed</u>
Process		
cholesterol homeostasis	IMP	PubMed
cholesterol metabolism	IMP	PubMed
lipid transport	ŒΑ	
lipoprotein metabolism	IEA	
response to oxidative stress	IMP	<u>PubMed</u>
transport	IEA	
Component		
chylomicron	IEA	
extracellular region	IEA	

Homology:

Human, Rat

Map Viewer

extracellular space

Pathways

KEGG pathway: Alzheimer's disease 05010

KEGG pathway: Neurodegenerative Disorders <u>01510</u>

RCA PubMed

General protein information

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Name: apolipoprotein E

NCBI Reference Sequences (RefSeq)

7 🛊

mRNA Sequence NM 009696

Source Sequence BC028816

Product NP 033826 apolipoprotein E

Conserved Domains (1) summary

pfam01442: Apolipoprotein; Apolipoprotein A1/A4/E family

Location: 33 - 276 Blast Score: 604

7 🛊 Related Sequences Nucleotide Protein Strain Genomic D00466 BAA00361 BALB/c **mRNA** None C57BL/6J AK010261 **mRNA** <u>AK019319</u> None C57BL/6J **mRNA** AK075843 BAC36000 C57BL/6J **mRNA** <u>AK 13 1624</u> None C57BL/6J **mRNA** AK134921 BAE22338 C57BL/6J **mRNA** AK148747 None C57BL/6J **mRNA** AK149111 BAE28740 C57BL/6J **mRNA** AK149568 BAE28964 C57BL/6J AK150834 **mRNA** BAE29894 C57BL/6J **mRNA** AK159105 BAE34821 C57BL/6J **mRNA** AK159424 BAE35071 C57BL/6J **mRNA** AK159517 BAE35147 C57BL/6J **mRNA** BC028816 AAH28816 FVB/N BC044785 **mRNA** None FVB/N **mRNA** BC083351 AAH83351 C57BL/6 **mRNA** CT010212 CAJ18420 **mRNA** CT010356 CAJ18564 **mRNA** M12414 AAA37251 **mRNA** M73490 AAA37252 C57BL/6J None <u>P08226</u> **Additional Links** 7 🛊 UniGene Mm.305152 Gene Expression Database (GXD) at MGI MGI:88057

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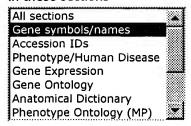


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Other Genome Feature Detail

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Dotan				
Symbol	Tg(GFAP-APOE4)			
Name ID	THOI transgene insertion 1, David M Holtzman MGI:3057183 Nomenclature History			
Genetic Map	Chromosome Unknown			
Phenotypes	All phenotypic alleles(1): Transgenic(1)			
References	<u>J:93487</u> Sun Y <i>et al.</i> , "Glial fibrillary acidic protein-apolipoprotein E (apoE) transgenic mice: astrocyte-specific expression and differing biological effects of astrocyte-secreted apoE3 and apoE4 lipoproteins." J Neurosci 1998 May 1;18(9):3261-72 All references(1)			

last database update 11/07/2005 MGI 3.4